Reports of Biochemistry & Molecular Biology
Vol.4, No.2, Apr 2016

Original article **www.RBMB.net**

Parthenolide Induces Apoptosis in Committed Progenitor AML Cell line U937 via Reduction in Osteopontin

Mahdi Zahedpanah[1], Mojgan Shaiegan*[1], Seyed Hamidollah Ghaffari*[2], Mohsen Nikbakht[2], Mahin Nikugoftar[1], Saeed Mohammadi[1]

Abstract

Background: Interfering with cell proliferation and survival is a critical role for antineoplastic drugs leading to cell death through induction of apoptosis. Alternative treatments with herbal extracts offer insights into acute myeloid leukemia (AML) therapy. Parthenolide (PTL), an extract from feverfew, induces apoptosis in primary human leukemia stem cells (LSCs) and bulk leukemic cell populations. Osteopontin (OPN) preserves cell viability in response to anticancer agents and its receptors could be utilized for therapeutic targeting of cancer cells.

Methods: U937 cells were cultured in RPMI 1640 with concentrations of 2, 4, 6, 8, and 10 µM PTL for 20-24 hours for MTT assays. Apoptosis assays were performed with Annexin V-Alexa Fluor-488/PI as Annexin V+/PI- and Annexin V+/PI+ to measure early and late apoptosis, respectively. Quantitative real-time PCR was used to measure OPN gene expression using the $2^{-\Delta\Delta Ct}$ method. The PTL–treated cells were stained with FITC-CD38 antibody for flow cytometry analyses. Data were compared using one-way analysis of variance (ANOVA) by SPSS 19.

Results: Parthenolide inhibited growth of U937 cells with IC25 and IC50 values of 4 and 5.8 µM, respectively. Death induction with PTL was apoptotic. Flow cytometry showed a significant decrease in the percentage of CD38+ U937 cells in response to PTL. Osteopontin gene expression decreased in response to PTL.

Conclusions: PTL induced apoptosis and reduced OPN gene expression in U937 cells.

Keywords: AML cell line U937, Osteopontin, Parthenolide

Introduction

Acute myeloid leukemia (AML) is a clonal disorder through transformation and uncontrolled proliferation of myeloid progenitor cells with arrested differentiation (1). Leukemic stem cells (LSCs) are AML-initiating cells of various populations with different features (2, 3). Acute myeloid leukemia-initiating cells are identified immunophenotypically as CD34+ and CD38- or CD34+ and CD38+ (4, 5). As AML cells mature, CD34 expression decreases gradually while CD38+ increases (6, 7). Current AML treatment utilizes chemotherapy with cytarabine and an anthracycline to achieve complete remission (CR) (8). Most therapies target molecules involved in

1: Blood Transfusion Research center, High Institute for Research and Education in Transfusion Medicine, Tehran, Iran
2: Hematology, Oncology and Stem Cell Transplantation Research Center, Shariati Hospital, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran.
***Corresponding authors: Mojgan Shaiegan; Tel: +982188601572; Fax: +982188601573; M.Shaiegan@ibto.ir**
Seyed Hamidollah Ghaffari; Tel: +982184902665; Fax: +982188004140; ghaffari200@yahoo.com
Received: Nov 16, 2015; Accepted: Jan 8, 2016